

The diagram illustrates the differentiation and proliferation of NS-IC (Neural Stem/Injury Cells). At the top, a single cell labeled "NS-IC" is shown. An arrow points down to a cluster of cells labeled "NEUROSPHERE". From the "NEUROSPHERE", two arrows point downwards to the left, labeled "DIFFERENTIATION". These arrows lead to three distinct cell types: "ASTROCYTE", "NEURON", and "OLIGODENDROCYTE". To the right of the "NEUROSPHERE", an arrow points to a group of cells labeled "NS-IC", with a curved arrow indicating a feedback loop back to the "NEUROSPHERE". This process is labeled "PROLIFERATION". A note next to the proliferating cells states: "NEUROSPHERE PROGENY ARE ENRICHED IN AC133<sup>+</sup> CELLS".

FIG. 1

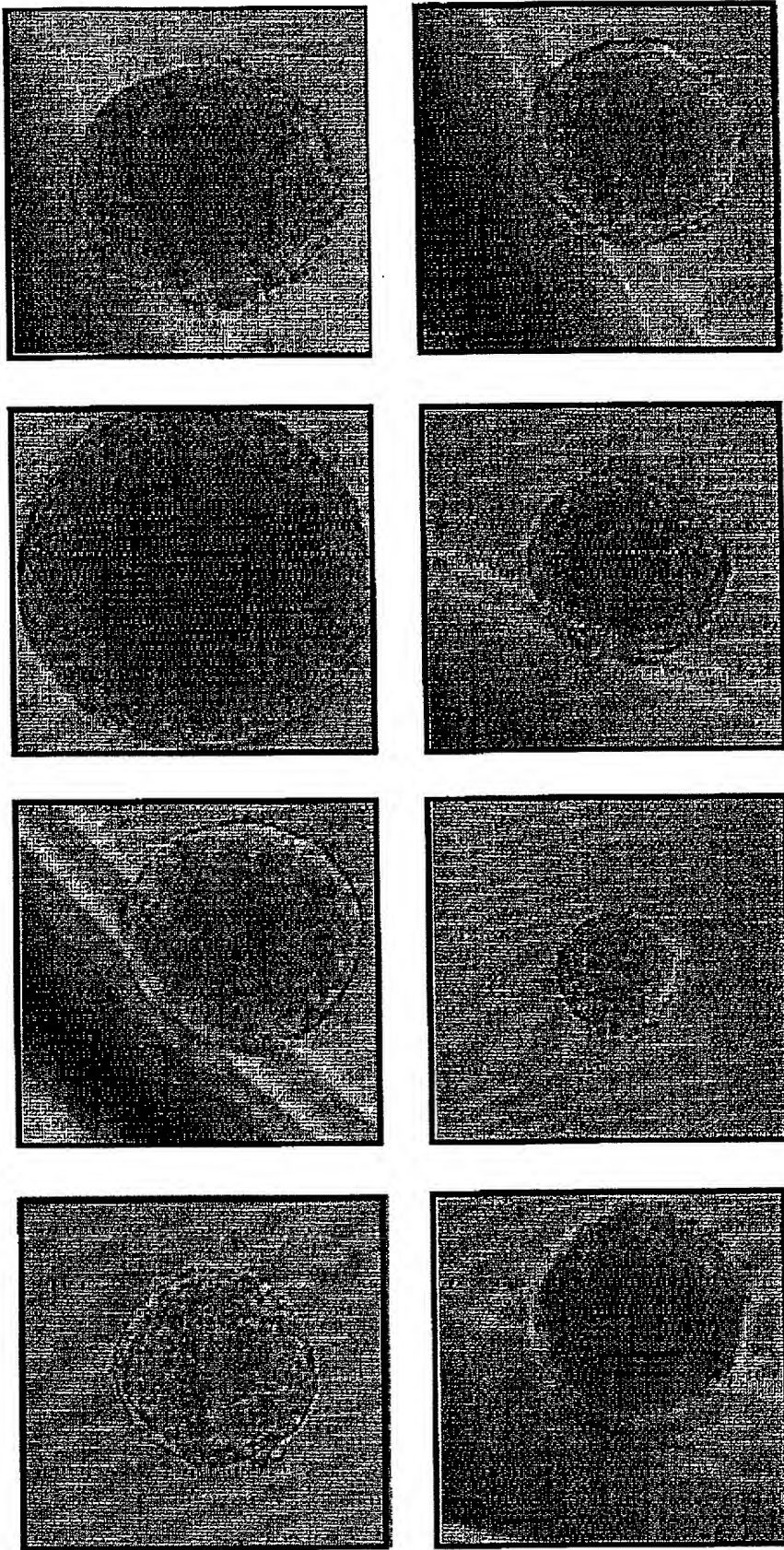
*Fig. 2*

FO6080-2FO22660

## Clonal Expansion of Neural Stem/Progenitor Cells

- Neurospheres can be derived from single-cell sorted 5F3<sup>+</sup> cells

**Week 8 NS-IC, 1 cell/well**



**FBR 1209 (16 G.W.)**

**20x**

# Isolation of Human Neural Stem Cells by Cell Surface Markers

Neurosphere initiating cells can be separated using monoclonal antibody 5E12

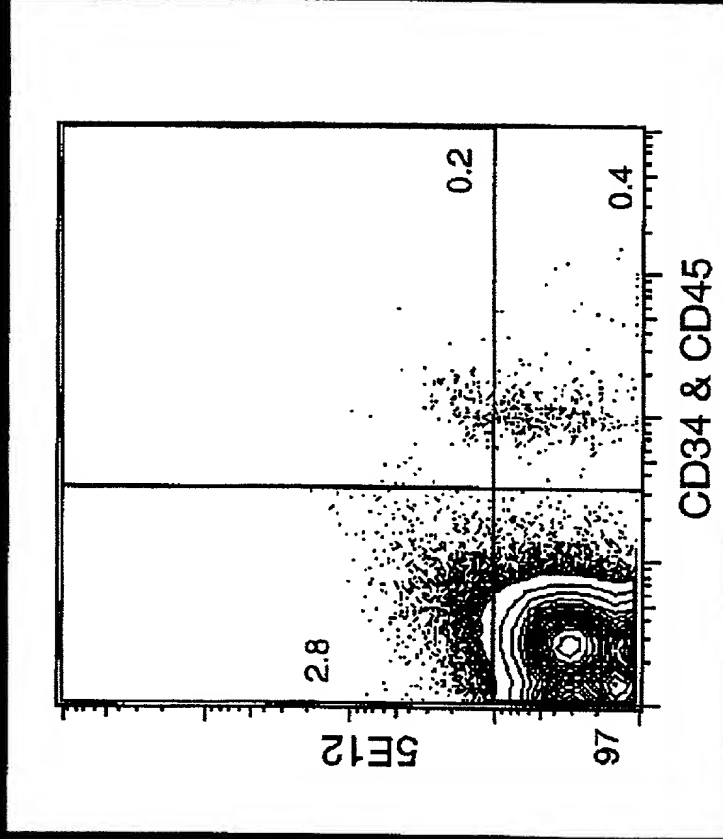


Fig. 3

# Isolation of Human Neural Stem Cells by Cell Surface Markers

Negative Marker for NSCs

Co-expressed on 5F3+ cells

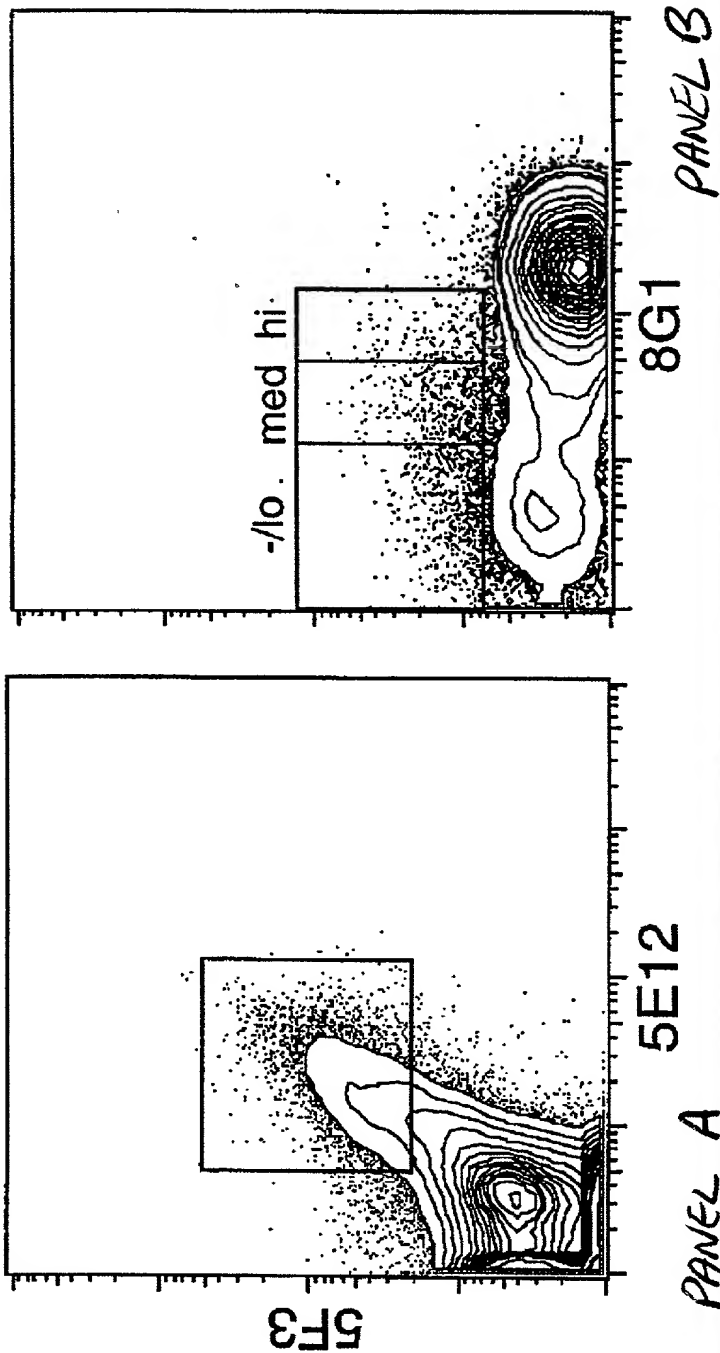


FIG. 4

## Distribution of 5F3+ cells in fetal brain

- ◆ The frequency of 5F3+ cells is lower at later gestational ages.
  - Extensive proliferation of non-stem cells compartment?
  - Need additional surface marker to subset 5F3+ cells?

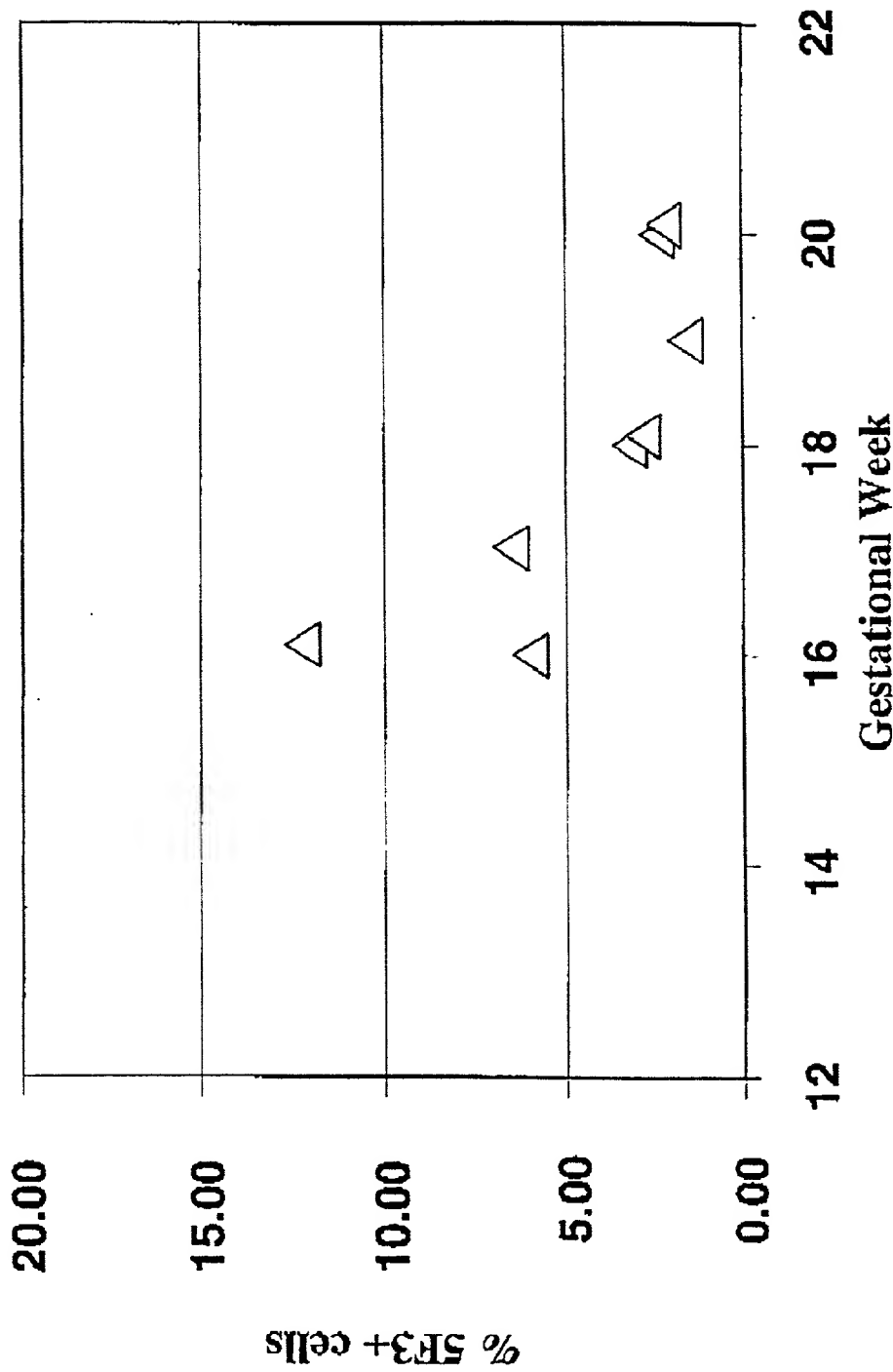
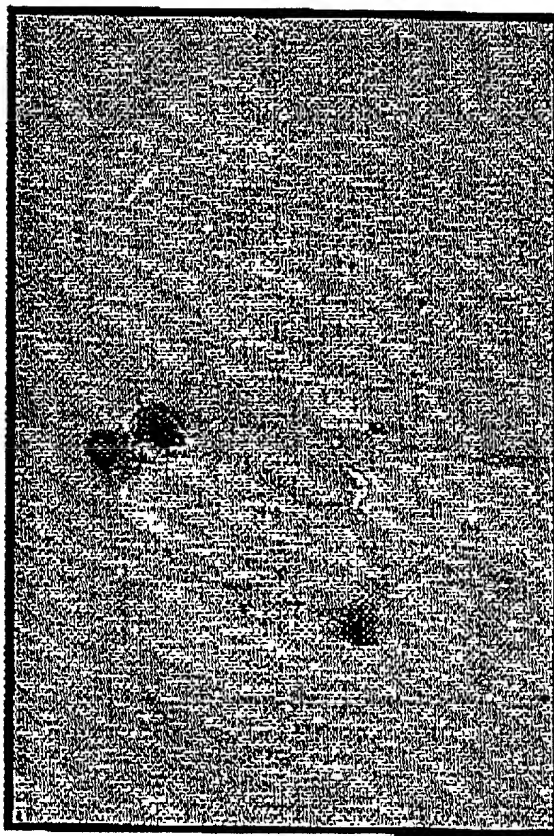
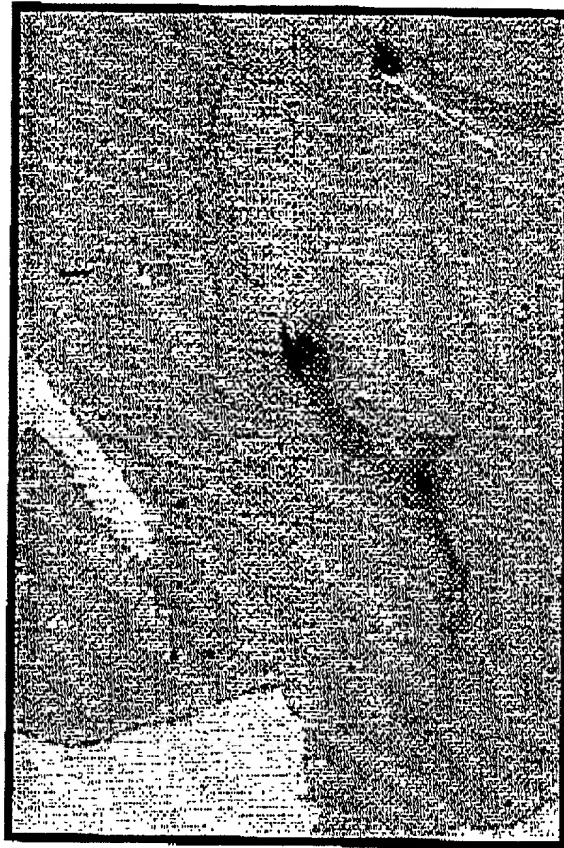


Fig. 5

FOUO "2FO22660

## In vivo studies: Transplantation into NOD SCID mouse

- Human neural cells can be transplanted into the lateral ventricle of neonatal immunodeficient mice
- Engraftment and migration of human neurosphere cells were detected between 4-8 weeks after injection using a human specific Thy-1 antibody



PROPRIETARY & CONFIDENTIAL

Fig. 6

Print  
10/15/99

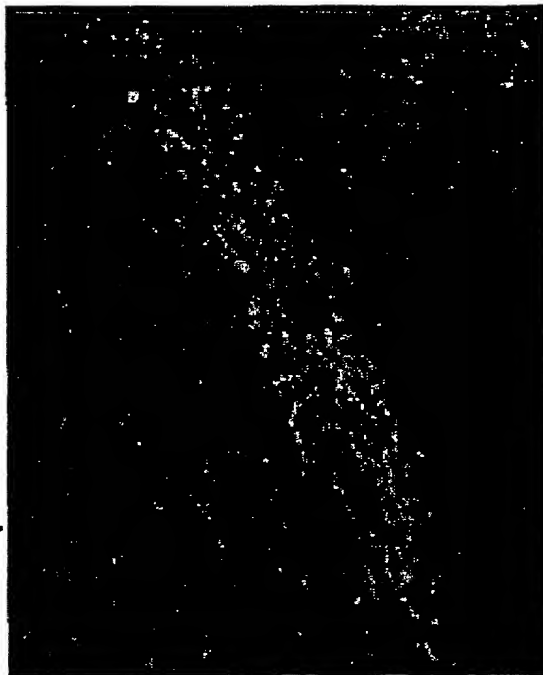
T06080"2T042660

## Progeny of 5F3<sup>+</sup> Sorted Neurosphere Cells Migrate through the RMS

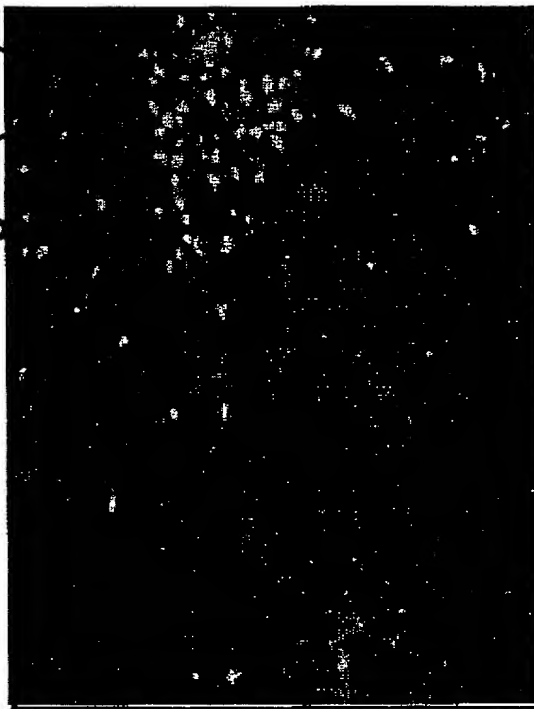


4x

Human  $\beta$ -tubulin in the RMS (20x)



Human nuclear antigen (20x)



5F3<sup>+</sup> sorted neurosphere cells (p8) , 7 months post transplant

FIG. 7

*Handwritten:*  
p8

T06080" 2F022660

## Migration of Human Neural Cells into Olfactory Bulb

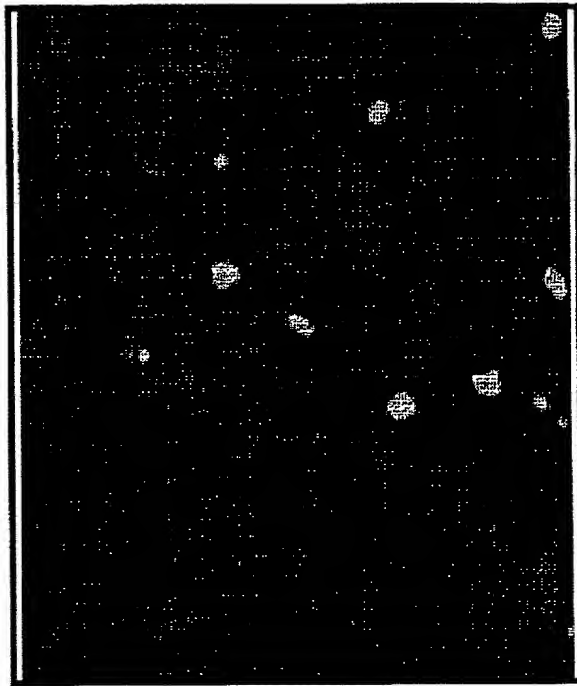
- Progeny of 5F3+ sorted neurosphere cells migrated through the RMS into Olfactory Bulb.

human nuclear antigen

(10x)



(40x)



5F3+ sorted neurosphere cells (p8) . 7 months post transplant

FIG. 8